CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

P-MENTHANE-3,8-DIOL

Chemical Code # 5255, Tolerance # 52349

3/24/99

I. DATA GAP STATUS

Chronic toxicity, rat:	No study on file; not required at this time[1]
Chronic toxicity, dog:	No study on file; not required at this time[1]
Oncogenicity, rat:	No study on file; not required at this time[1]
Oncogenicity, mouse:	No study on file; not required at this time[1]
Reproduction, rat:	No study on file; not required at this time[1]
Teratology, rat:	No data gap; No adverse effect
Teratology, rabbit:	No study on file; not required at this time[1]
Reverse gene mutation:	No data gap; No adverse effect
Forward gene mutation:	No data gap; No adverse effect
In vivo cytogenetics:	No data gap; No adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 158943 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T169969
Leung, 3/24/99

[1] Toxicology data for p-menthane-3,8-diol have been submitted and reviewed as a biochemical pesticide. Toxicity data requirements are set forth under a tiered system. These studies are not required at this time.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

No study on file.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

012;158943; “Rat Prenatal Developmental Toxicity Study with Granola 97 (SCJ NB# 14735R108)” (A. E. Wakefield; Covance Laboratories, Inc., Vienna, VA; Lab Report No. 6106-116; 10/30/97); Granola 97 (Lot. No. 703002; purity = 98.5%), applied undiluted (after heating to 98EF) to groups of 25 mated Crl:CD rats at dose levels of 0 (H_2O), 1, or 3 g/kg/day on days 6-19 of gestation; dermal exposure, 6-7 hours/day, occlusive wrap; no unscheduled deaths; slightly decreased weight gain in the high-dose group during the treatment period; 2/23 dams in the low-dose group had small litters (2-3 implants) that were completely resorbed; no treatment-related effects on pregnancy outcomes or the incidence of fetal abnormalities; **no adverse effects; maternal NOEL = 1 g/kg/day (decreased weight gain); developmental NOEL = 3 g/kg/day (no effects observed at HDT); **Acceptable.** (Duncan, 3/26/98)

TERATOLOGY, RABBIT

No study on file.

REVERSE GENE MUTATION

007; 158938; "Bacterial Reverse Mutation Assay with Granola 97 (SCJ NB# 14735R108)"; (V. O. Wagner and E. W. Watson; MA BioServices, Inc., Rockville, MD; Lab Study No. G97BF49.502; 11/18/97 (amended report II); Granola 97 (Lot. No. 703001; purity = 98.3%), dissolved in DMSO, was tested in the bacterial reverse mutation assay using *S. typhimurium* TA98, TA100, TA1535, TA1537, and *E. coli* WP2uvrA with and without metabolic activation (Aroclor 1254-induced rat liver S9 fraction), by plate incorporation; one trial was conducted over a dose range of 75-5000 ug/plate (*S. typhimurium*) or 25-5000 (*E. coli*) with triplicate plates for each treatment; **no adverse effects; no significant increase in mutation frequency was

observed; positive controls were functional; **Acceptable.** (Duncan, 4/20/98)

FORWARD GENE MUTATION

006; 158937; "*In Vitro* Mammalian Cell Gene Mutation Test with Granola 97 (SCJ NB# 14735R108)"; (R. H. C. San and J. J. Clarke; MA BioServices, Inc., Rockville, MD; Lab Study No. G97BF49.702; 11/20/97 (amended report II); L5178Y/TK$^{+/-}$ mouse lymphoma cells were exposed for four hours to Granola 97 (Lot. No. 703001; purity = 98.3%) dissolved in DMSO; one trial was conducted over a dose range of 600-1500 ug/ml (non-activated) and 500-1250 ug/ml (activated) with duplicate cultures at each dose level; MMS (10, 20 ug/ml) and DMBA (2.5, 4.0 ul/ml) were used as control materials; activation source was Aroclor 1254-induced rat S9 liver homogenate fraction; **no adverse effects; precipitation in the growth medium and cytotoxicity were observed at concentrations of approx. 1500 ug/ml and above; no significant increase in mutation frequency was observed; positive controls were functional; **Acceptable.** (Duncan, 4/8/98)

009; 158940; "*In Vitro* Mammalian Cytogenetic Test Using Chinese Hamster Ovary (CHO) Cells with Granola 97 (SCJ NB# 14735R108)"; (R. Gudi and E. Schadly; MA BioServices, Inc., Rockville, MD; Lab Study No.G97BF49.335; 11/20/97 (amended report II); CHO-K_1 cells were treated with Granola 97 (Lot. No. 703001; purity = 98.3%) diluted in DMSO in two separate trials for periods of 6 h (w/ and w/o activation), 20 h or 44 h (w/o activation); Aroclor 1254-induced rat liver S9 fraction was the source of activation; all assays were performed in duplicate cultures and appropriate positive and negative controls were tested concurrently; 200 metaphases/ treatment were scored for aberrations; no biologically significant increases in chromosome aberrations in non-activated cultures; in activated cultures, a weakly clastogenic effect at 250, 500, 1000, and 1500 ug/ml was observed at the 44-h harvest; However, the percentage of cells with structural aberrations were within historical control values (0-6%) for negative controls. Therefore, this effect was not considered to be toxicologically significant. **No adverse effects; Acceptable. (Duncan, 4/22/98)

IN VIVO CYTOGENETICS

008; 158939; "Mammalian Erythrocyte Micronucleus Test with Granola 97 (SCJ NB# 14735R108)"; (R. Gudi and P. Ritter; MA BioServices, Inc., Rockville, MD; Lab Study No. G97BF49.123001; 11/20/97 (amended report II); Granola 97 (Lot. No. 703001; purity = 98.3%), was diluted in corn oil and dosed by ip injection to groups of five ICR mice/sex/treatment at 0 (vehicle), 104, 208, and 416 mg/kg, and by dermal application at 3 ml/kg/day (four applications); bone marrow was collected at 24 h in all groups and additionally at 48 h in the vehicle and high-dose groups; 2000 polychromatic erythrocytes/animal were scored for micronuclei; **no adverse effects were observed; no increase in micronucleated PCEs was observed; cyclophosphamide was functional in the assay. **Acceptable.** (Duncan, 4/20/98)

NEUROTOXICITY

Not required at this time.

SUBCHRONIC STUDIES

011;158942; “A 90-Day Dermal Toxicity Study of Granola 97 in Rats” (R. E. Rush; Springborn Laboratories, Inc., Spencerville, OH; Lab Study No. 3068.63; 10/14/97); Granola 97 (Lot. No. 703001; purity = 98.3%), applied undiluted at 37-45EC; 0 (dH2O), 1000, 3000 mg/kg/day; 15 CD rats/sex/dose level; applied 7 d/wk, except during intervals when functional observation battery was performed, for 90 d; occlusive wrap, 6-hour/day exposure; five deaths, all related to wrapping; moderate dermal irritation (erythema, mild or focal eschar, desquamation), increased relative liver weight in high-dose males and females (without histological changes), and increased kidney weight in high-dose males with histological changes

consistent with alpha-2u-globulin nephropathy; **no adverse effects;** NOEL (M and F) = 1000 mg/kg/day (increased relative liver weights); **Acceptable.** (Duncan, 3/4/98)

010; 158941; "Immunotoxicity Screening Study in Mice Exposed Dermally to Granola 97" (R. V. House, W. D. Johnson, J. F. Krueger; IIT Research Institute, Chicago, IL; Lab Project No. L08686; 10/17/97); Granola 97 (Lot. No. 703001; purity = 98.3%), was applied undiluted to 10 female B6C3F1 mice/group in 28 daily dermal doses at 1 and 3 g/kg/day; a vehicle control group was dosed with dH_2O and a positive control group was injected ip with cyclophosphamide on day 28; animals were induced with a single injection of sheep red blood cells (SRBC) on day 25, thymuses and spleens were collected on day 29; the anti-SRBC antibody-forming cell assay was performed with spleen cells on day 29; **no adverse effects indicated**; an increase in AFC/10^6 viable spleen cells was observed in the low-dose group, but not the high-dose group; due to lack of hematology, histopathological exam, clinical chemistry, specific and non-specific cell-mediated immunity assays, this study is **unacceptable and not upgradeable.** (Duncan, 4/23/98)